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13780-2/226A/CO93.US.CP2

Avenue, 9<sup>th</sup> Floor, Pasadena, California 91101, as directed in the Declaration and Power of Attorney Form filed with the US Patent and Trademark Office on April 2, 2002.

### CONCLUSION

If there are any issues that can be resolved by telephone with the Applicants representative, the Examiner is encouraged to contact the undersigned directly.

The Commissioner is hereby authorized to charge payment of \$434 (\$130 for the one month extension and \$324 for the additional claim fees) to Deposit Account No. 19-2090. The Commissioner is further authorized to charge any other fees or credit any overpayment associated with this Response and Amendment to Deposit Account No. 19-2090.

Respectfully Submitted,

SHELDON & MAK  
a Professional Corporation

Date: 8/21/02By 

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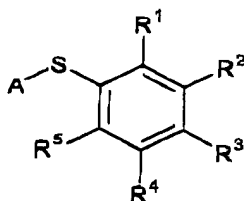
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## SPECIFICATION AMENDMENTS WITH MARKINGS TO SHOW CHANGES

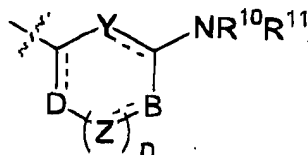
Beginning on page 4, line 8 and ending on page 6, line 14:

The present invention is directed to compounds of [the structure] Formula I

Formula I

or pharmaceutically acceptable salts, optical isomers, or prodrugs thereof,

wherein R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup> and R<sup>5</sup> are each independently selected from the group consisting of hydrogen, halogen, alkyl, haloalkyl, alkoxy, cyano, nitro, cycloalkyl, [and] carboxaldehyde[;], and a group of Formula II defined as:

[with the proviso that at least one of R<sup>1</sup> or R<sup>3</sup> is]

Formula II

subject to the proviso that one or more than one of R<sup>1</sup> or R<sup>3</sup> is a group ofFormula II as defined above;

wherein D, B, Y and Z at each occurrence are independently selected from the group consisting of -CR<sup>6</sup>=, -CR<sup>7</sup>R<sup>8</sup>-, C(O)-, -O-, -SO<sub>2</sub>-, -S-, -N=, and -NR<sup>9</sup>-;

n is an integer of zero to three;

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R<sup>6</sup>, R<sup>7</sup>, R<sup>8</sup>, and R<sup>9</sup>, at each occurrence, are each independently selected from the group consisting of hydrogen, alkyl, carboxy, hydroxyalkyl, alkylaminocarbonyl, alkyl, dialkylaminocarbonylalkyl and carboxyalkyl; and

R<sup>10</sup> and R<sup>11</sup> are each independently selected from the group consisting of hydrogen, alkyl, cycloalkyl, alkoxyalkyl, alkoxycarbonylalkyl, carboxyalkyl, hydroxyalkyl, heterocyclyl, heterocyclylalkyl and heterocyclylamino; or

[wherein] R<sup>10</sup> and R<sup>11</sup> are taken together with N [may be joined] to form a three to seven membered unsubstituted heterocyclyl ring, or a three to seven membered substituted heterocyclyl ring, [said ring being optionally] substituted with one or more than one substituent [substituents] R<sup>13</sup>, wherein R<sup>13</sup>, at each occurrence is independently selected from the group consisting of alkyl, alkylene, alkoxy, alkoxyalkyl, cycloalkyl, aryl, heterocyclyl, heterocyclylalkyl, heterocyclylcarbonyl, heterocyclylalkylaminocarbonyl, hydroxy, hydroxyalkyl, hydroxyalkoxyalkyl, carboxy, carboxyalkyl, carboxycarbonyl, carboxaldehyde, alkoxycarbonyl, arylalkoxycarbonyl, aminoalkyl, aminoalkanoyl, aminocarbonyl, carboxamido, alkoxycarbonylalkyl, carboxamidoalkyl, cyano, tetrazolyl, alkanoyl, hydroxyalkanoyl, alkanoyloxy, alkanoylamino, alkanoyloxyalkyl, alkanoylaminoalkyl, sulfonate, alkylsulfonyl, alkylsulfonylaminocarbonyl, arylsulfonylaminocarbonyl and heterocyclylsulfonylaminocarbonyl;

wherein A is an unsubstituted aryl [or] group, an unsubstituted heterocyclyl group, a substituted aryl group, or a substituted heterocyclyl group, substituted with one or more than [said aryl or heterocyclyl group having at least] one substituent R<sup>12</sup>, wherein R<sup>12</sup>, at each occurrence, is independently selected from the group consisting of [hydrogen,] halogen, alkyl, aryl, haloalkyl, hydroxy, alkoxy, alkoxyalkyl, alkoxycarbonyl, alkoxyalkoxy, hydroxyalkyl, aminoalkyl, aminocarbonyl, alkyl(alkoxycarbonylalkyl) aminoalkyl, heterocyclyl,

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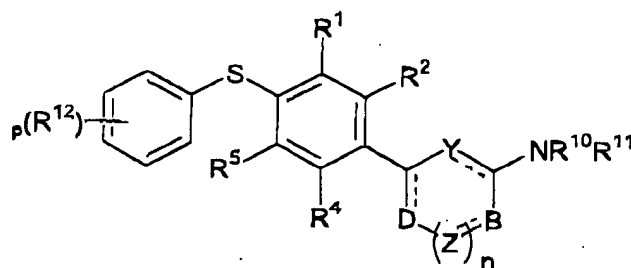
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heterocyclalkyl, carboxaldehyde, carboxaldehyde hydrazone, carboxamide, alkoxycarbonylalkyl, carboxy, carboxyalkyl, carboxyalkoxy, carboxythioalkoxy, carboxycycloalkoxy, thioalkoxy, carboxyalkylamino, trans-cinnamyl, hydroxyalkylaminocarbonyl, cyano, amino, heterocyclalkylamino, and heterocyclalkylaminocarbonyl; and

wherein  $R^1$ ,  $R^2$ ,  $R^3$ ,  $R^4$ ,  $R^5$ ,  $R^6$ ,  $R^7$ ,  $R^8$ ,  $R^9$ ,  $R^{10}$ ,  $R^{11}$ ,  $R^{12}$  and  $R^{13}$  are unsubstituted or substituted with at least one electron donating or electron withdrawing group; [or a pharmaceutically-acceptable salt, optical isomer or prodrug thereof].

Beginning on page 6, line 18 and ending on page 8, line 16:

The present invention is also directed to compounds of [the structure] Formula III



Formula III

wherein  $R^1$ ,  $R^2$ ,  $R^3$ ,  $R^4$  and  $R^5$  are each independently selected from the group consisting of hydrogen, halogen, alkyl, haloalkyl, alkoxy, cyano, nitro, cycloalkyl and carboxaldehyde;

D, B, Y and Z are as defined above for Formula I;

$R^{12}$ , at each occurrence, is independently selected from the group consisting of [hydrogen,] halogen, alkyl, haloalkyl, alkoxy, carboxyalkoxy, carboxyalkyl and heterocyclalkyl; and[,]

p is an integer of zero to five;

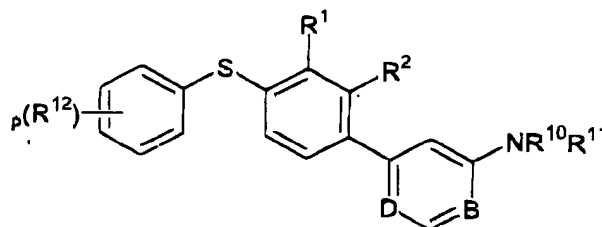
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wherein  $R^1$ ,  $R^2$ ,  $R^4$ ,  $R^5$ ,  $R^{10}$ ,  $R^{11}$  and  $R^{12}$  are unsubstituted or substituted with at least one electron donating group or electron withdrawing group.

Presently most preferred, but not required, compounds of Formula III have  $p$  as one;  $R^4$  and  $R^5$  as hydrogen;  $R^{12}$  as halogen, alkyl, carboxyalkoxy, carboxyalkyl or heterocyclyl; and  $R^{10}$  and  $R^{11}$  [joined] are taken together with N to form a three to seven membered unsubstituted heterocyclyl ring, or a three to seven membered substituted heterocyclyl ring; said ring being piperidine, piperazine, morpholine, pyrrolidine or azetidine.

Presently most preferred, but not required, compounds are of [the structure] Formula IV



Formula IV

wherein D and B are each independently selected from the group consisting of  $-N=$  and  $-CR^6=$ ;

$R^1$  and  $R^2$  are each independently selected from the group consisting of hydrogen, halogen and haloalkyl;

$R^{10}$  and  $R^{11}$  are as defined above for Formula I;

$R^{12}$ , at each occurrence, is independently selected from the group consisting of [hydrogen], halogen, alkyl, haloalkyl, alkoxy, carboxyalkoxy, carboxyalkyl and heterocyclyl;

$p$  is an integer of zero to five; and[,]

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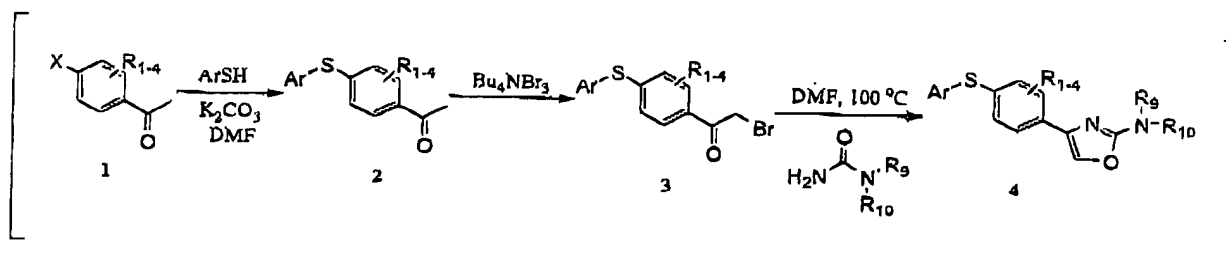
wherein  $R^1$ ,  $R^2$ ,  $R^{10}$ ,  $R^{11}$ , and  $R^{12}$  are unsubstituted or substituted with at least one electron donating group or electron withdrawing group.

[For presently] Presently most preferred, but not required, compounds are of Formula IV, where p [may] can be one;  $R^{12}$  [may] can be halogen, alkyl, alkoxy, carboxyalkoxy, carboxyalkyl or heterocyclyl; and  $R^{10}$  and  $R^{11}$  [may] can be [joined] taken together with N to form a three to seven membered heterocyclyl ring; said ring being piperidine, piperazine, morpholine, pyrrolidine or azetidine.

Beginning on page 28, line 10 (with the words "Scheme I"), and ending on page 31, line 10:

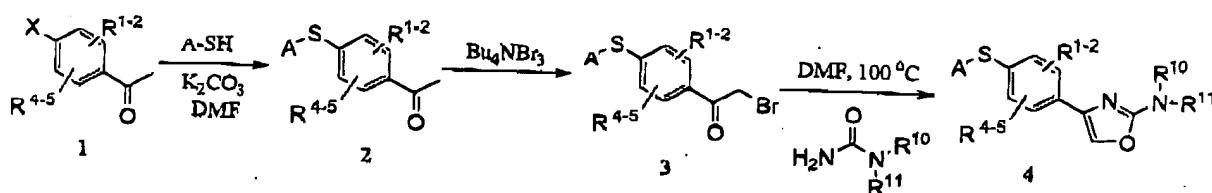
Scheme [I] 1 describes compounds of Formula I which contain an oxazole ring ( $n=0$ ,  $Y=N$ ,  $B=O$ ,  $D=C$ ). In Scheme 1, and likewise in Schemes 2 and 4, the substituent X is a leaving group. In Scheme I, aryl [Aryl] methyl ketone 1, with [the] an appropriate substitution ( $R_{1-2}$  and  $R_{4-5}$ ), and a leaving group  $X$ , reacts with an aryl thiol to give a biaryl sulfide 2. Biarylsulfide 2 can be converted into an alpha-bromomethyl ketone 3 using a variety of reagents including  $Bu_4NBr_3$ . Condensation of 3 with a urea [then] gives a [the] desired [compounds] oxazole compound 4.

### Scheme 1



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Another method of preparing compounds of Formula I containing an oxazole ring ( $n=0$ ,  $Y=N$ ,  $B=O$ ,  $D=C$ ) is illustrated in Scheme 2. In Scheme 2, an aryl [Aryl] methyl ketone [ketones] 1 is [1 are] converted into an alpha-hydroxymethyl ketone 5, which then can be reacted with an arylthiol [arylthiols] to give a biaryl sulfide 6. Acid-catalyzed condensation of 6 with KOCN affords a 2-hydroxy oxazole 7, which can be converted into a 2-chloro-oxazole 8 using  $POCl_3$ . Displacement of the chloride of 8 with an amine [amines] gives a [the] desired 2-amino-oxazole 9.

Scheme 2